PROC (BAYL UNIV MED CENT)
2022;35(2):243–244

https://doi.org/10.1080/08998280.2021.1994909

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Synchronous development of prostate sarcoma and squamous cell carcinoma following radiotherapy

Vihitha Thota, MD[a], Keerthy Joseph, DO[a], Sudheer Konduru, MD[a], Manaswitha Thota, BS[b], and Eugene J. Choi, MD[c]

[a]Department of Internal Medicine, Mercy Catholic Medical Center, Darby, Pennsylvania; [b]School of Medicine, Virginia Commonwealth University, Richmond, Virginia; [c]Department of Hematology and Oncology, Mercy Catholic Medical Center, Darby, Pennsylvania

ABSTRACT

With the development of more sensitive screening tools, malignancies are being diagnosed at an earlier stage, resulting in earlier intervention and longer survival times. As a consequence, the long-term complications of cancer therapy are increasing in incidence, particularly second primary cancers from radiation therapy. Bladder and colorectal cancers are the most commonly reported malignancies secondary to radiation therapy for prostate cancer. We present the case of a 78-year-old patient with a remote history of prostate adenocarcinoma, status post brachytherapy, who subsequently developed both prostate sarcoma and prostate squamous cell carcinoma secondary to the prior treatment. Because his cancer was metastatic, he was not a candidate for surgery and was treated with chemotherapy and palliative radiation.

KEYWORDS Low-dose brachytherapy; prostate sarcoma; prostate squamous cell carcinoma; radiation-induced malignancies; second primary cancer

Clinical advancements in cancer treatments have revolutionized the field of oncology in recent decades, resulting in improved outcomes and longer survival times. A primary treatment option for localized prostate cancer is brachytherapy,[1] a form of radiation therapy that involves the implantation of radioactive seeds into the prostate with radiation emitted over several months; this enhances the therapeutic ratio by allowing a higher radiation concentration in cancer cells.[2] With the increased utilization of radiation therapy, the incidence of associated complications has risen, including radiation-induced malignancies such as prostate sarcomas and squamous cell carcinomas,[3] particularly in patients treated with radiation therapy for prostate adenocarcinoma. Both prostate sarcoma and prostate squamous cell carcinoma are rare malignancies on their own; their coexistence in the same individual has not yet been reported. We present the unique case of interval diagnosis of both prostate sarcoma and prostate squamous cell carcinoma in a patient with a remote history of prostate adenocarcinoma.

CASE PRESENTATION

A 78-year-old African American man, with known prostate adenocarcinoma treated with low-dose brachytherapy over 15 years ago without recurrence, presented with acute urinary retention and a 20-pound weight loss over a 1-month period. Urinalysis was notable for hematuria, and a bladder scan revealed an elevated postvoid residual. His prostate-specific antigen level was <0.008 ng/mL, and imaging revealed a large mass protruding posteriorly from the prostate with intrusion into the rectum *(Figure 1a)*, along with an adjacent 5-cm pelvic mass, new enlarged pelvic side-wall lymph nodes, a left common iliac lymph node, and a right lung nodule suspicious for metastatic disease. He underwent cystoscopy and transurethral resection of the prostate, with pathology revealing bizarre-appearing tumor cells positive for vimentin and focal CD68 and AE1/AE3 and negative for PSA, PSAP, GATA3, p63, uroplakin, CK903, and desmin; this was consistent with high-grade sarcoma of the prostate *(Figure 1b)*. Given concern for radiation-induced prostate sarcoma with metastatic disease, he was not a candidate for either radiation or surgery. Therefore, chemotherapy with doxorubicin was initiated with a good response. Subsequent imaging 3 months later showed an interval decrease of the primary mass and associated lymphadenopathy with no new metastatic lesions.

Corresponding author: Vihitha Thota, MD, Department of Internal Medicine, Mercy Catholic Medical Center, 1500 Lansdowne Ave., Box #40, Darby, PA 19023 (e-mail: vihitha.thota@mercyhealth.org)

The authors report no conflicts of interest. Consent was obtained from the patient to publish his anonymized information in this article.
Received July 14, 2021; Revised October 10, 2021; Accepted October 11, 2021.

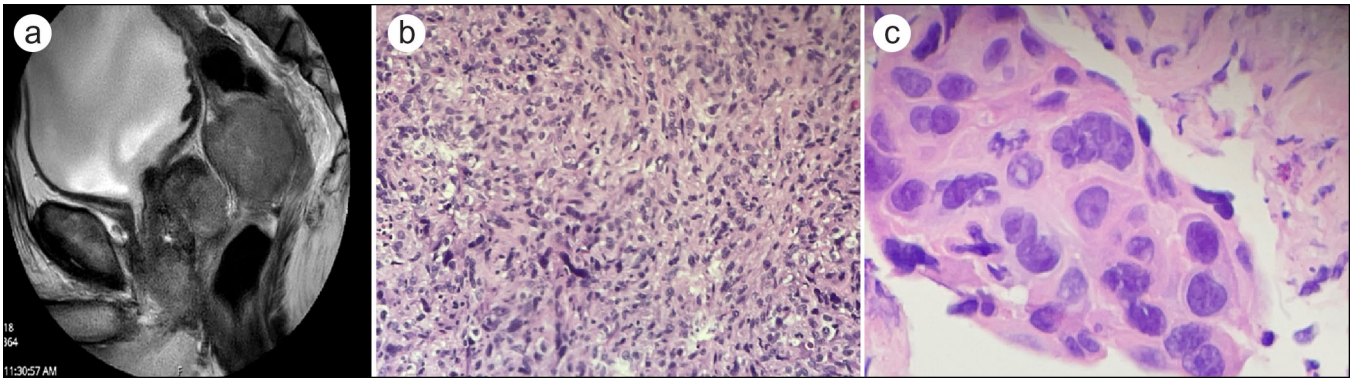

Figure 1. **(a)** Magnetic resonance imaging of the pelvis (T2W MVXD sagittal view) displaying a large prostatic mass causing bladder outlet obstruction and protrusion back/into the rectum. **(b)** Prostate biopsy revealing pleomorphic tumor cells consistent with high-grade prostate sarcoma. **(c)** Rectal biopsy showing cellular pleomorphism, abundant eosinophilic cytoplasm, and intercellular bridges, consistent with squamous cell carcinoma.

One month later, the patient presented with several episodes of bright red blood per rectum. His hemoglobin on admission was 4.8 g/dL with a hematocrit of 15.2%; his platelet count was stable at 391 k/μL. Repeat imaging revealed necrotic prostate cancer with residual pelvic lymph nodes; there was no evidence of new metastatic disease. He was transfused with multiple units of packed red blood cells, and colonoscopy revealed an ulcerated, partially obstructing, circumferential large mass in the rectum. Biopsy of the rectal mass *(Figure 1c)* revealed squamous cell carcinoma with tumor cells positive for p63 and CK5/6 and negative for CK20. Given the history of prostate cancer and prior imaging, the histopathologic findings were attributed to squamous cell carcinoma arising from the prostate with invasion into the rectum. Due to concern for rectal invasion causing recurrent bleeding, palliative radiation therapy was given with 30 Gy in 10 fractions to the rectal mass, with cessation of bleeding; following radiation therapy, the patient resumed chemotherapy with an improvement of disease burden.

DISCUSSION

Although radiation therapy is one of the primary modalities to treat a wide variety of cancers, the risk of developing radiation-induced malignancies as a long-term complication is a growing concern. A second primary cancer secondary to radiation exposure is diagnosed if the malignancy is (1) diagnosed after a >5-year latency period, (2) occurs within the field of therapy, (3) comprises a different histological type than the original cancer, and (4) was not present at the time of the initial therapy.[4] Both malignancies seen in our case met these criteria, leading to the etiology being attributed to radiation.

Both squamous cell carcinoma and sarcoma of the prostate are rare, comprising only 0.5% to 1%[1] and <1%[3] of all prostate cancers, respectively. These malignancies occurring secondary to radiation therapy are even more scarcely reported. Bladder cancer and colorectal cancer are the most common complications of radiation therapy for primary prostate cancer.[4] However, radiation-induced squamous cell carcinoma and sarcoma of the prostate, although very rare, are associated with a poor prognosis, with a median survival time of 14 months[2] and 18 months,[5] respectively. Given the aggressive nature of these malignancies, an equally aggressive and multimodal approach is taken with both surgery and neoadjuvant radiation plus or minus chemotherapy to improve outcomes.

This case is the first, to the best of our knowledge, to illustrate simultaneous diagnosis of both prostate sarcoma and squamous cell carcinoma in the same patient as a consequence of radiotherapy. Though the overall risk of developing secondary malignancy from radiation therapy remains small, the incidence is increasing. Particularly in the case of prostate cancer, the risk of mortality from a radiation-induced malignancy may be greater than the primary prostate tumor itself, especially as screening has resulted in an increased diagnosis of low-grade, less aggressive prostatic tumors that would likely never have resulted in complications from the cancer.

ORCID

Vihitha Thota http://orcid.org/0000-0001-5260-6213

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